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# Semantic factors influence multisensory pairing: a transcranial magnetic stimulation study

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It is traditionally assumed that temporal and spatial factors determine whether information provided by different sensory modalities is combined in a single percept. However, neuropsychological reports of selective damage to audio-visual integration and recent neurophysiological results suggest that semantic factors related to the content of the stimuli could also play a role. As a means of extending evidence provided by neuropsychological dissociations we set up a direct comparison of two kinds of audio-visual pairs with different semantic properties and used transcranial magnetic stimulation (TMS). We investigated the selective impact of TMS on two kinds of audio-visual pairings presented under identical

spatio-temporal conditions (face–voice and tone–shape pairings). Our results show that TMS applied over the left posterior parietal cortex at 200 ms disrupted audio-visual integration for the tone–shape pairings but not for the face–voice ones. Our data are consistent with neuropsychological findings and indicate that besides the well-known dimensions of spatial and temporal contiguity, content is an important determinant of audio-visual integration. Our study also illustrates the usefulness of TMS for addressing the role of semantic factors in multi-sensory perception *NeuroReport* 13:1567–1573 © 2002 Lippincott Williams & Wilkins.

**Key words:** Audio-visual pairings; Multi-sensory; Posterior parietal cortex; Single-pulse TMS

## INTRODUCTION

Hearing and seeing often provide information about the same external objects or events simultaneously. A noisily bouncing ball, a boisterous laughing face or a truck emitting beeps while making a reverse move are just a few of the many instances of audio-visual coincidence known in daily life. Such sensory coincidences create the perceptual impression of a unitary percept. This is presumably due to convergence between separate auditory and visual pathways in the brain [1] yielding rich multi-sensory percepts [2]. The traditional view in multi-sensory perception is that audio-visual pairings are predominantly based on structural factors like spatio-temporal contiguity. This operates as a kind of Gestalt creating the phenomenon of perceptual unity across two or more different sensory inputs [3–5] (see [6] for extensive discussion).

Another dimension, which also enters into pairing decisions and has received relatively little attention concerns the meaning of the stimuli or their semantic properties. For the present purposes we define semantics by reference to the common domain to which two stimuli from different sensory input systems belong. Examples are spatial information which is provided by vision, audition or touch; speech information provided by audition and vision (lip movements, gestures); and emotion (face expressions, voice intonations, gestures). The notion that domain specificity plays a role is consistent with what we learn from the

few neuropsychological studies on selective disruption of audio-visual integration that are available. Focal brain damage can selectively disrupt the perception of some audio-visual pairs and not others. For example, in a patient with bilateral occipito-temporal damage audio-visual integration was lost for speech but it remained intact for audio-visual emotion pairs [7]. Likewise, schizophrenics display a normal pattern of audio-visual integration in a ventriloquism task but not in an audio-visual speech task [8].

While the role of spatio-temporal factors in multi-sensory pairings has long been stressed, that of semantic factors like domain-specificity has been mostly ignored. Recent data from neurophysiological studies and brain-imaging methods suggest the existence of separate, content selective mechanisms of audio-visual integration. For example, brain-imaging data have shown that the amygdala plays a role in the integration of the auditory and visual parts of a fear stimulus [9]. In a PET study, the insula/claustrum was involved in cross-modal matching between visual and tactile modality [10]. fMRI data and cell-recordings in the monkey have indicated that the superior temporal sulcus plays a role for audio-visual speech pairs [11] and the posterior parietal cortex (PPC) is crucial for pairs like light flashes and sound bursts [12,13]. There is no study available yet to directly compare different multi-sensory pairings.

Transcranial magnetic stimulation (TMS) appears to be a suitable method for investigating domain specificity of audio-visual perception because it offers the opportunity to interfere selectively with processing in pre-determined brain areas. It allows us to extend neuropsychological findings about audio-visual perception in relation to lesion sites and to observe the functional equivalent of neuropsychological dissociations. TMS is designed to induce a transient current in brain regions underlying the skull by means of a brief magnetic pulse (single pulse method). The neural noise created by altering the local electric current in the underlying brain activity causes a functional deficit that is completely reversible (see [14] for a recent review). TMS allows interference during task performance and since interference can be created at specific neural sites and at specific latencies, condition specific effects and their time course can be measured.

Our goal was to compare two different audio-visual pairings presented under similar spatio-temporal conditions and to see whether site of TMS stimulation would selectively disrupt one type of pair and not the other. Based on the literature, we selected two types of audio-visual pairs, sound-shape and face-voice pairs. The modalities of perceptual integration and the underlying neuro-anatomical process of each pair have been studied previously and allowed clear *a priori* predictions. Electrophysiological results [15] have shown that interactions between sound (tone burst) and shape (geometrical figure) occurred early in time (< 200 ms post-stimulus onset) and were mainly manifested by amplification of exogenous modality-specific event-related brain potentials (such as the visual C1 component and the auditory N1 component). In a recent fMRI study [12] using sound-shape pairings (reversing black and white checkerboards paired with white noise bursts) cross-modal interactions were found in the superior colliculus as well as in a network of cortical brain areas including the insula, the superior temporal sulcus, the intraparietal sulcus and the superior and ventromedial frontal gyri. This recent brain-imaging study confirmed the involvement of the PPC (e.g. intraparietal sulcus) in multi-sensory integration of sound-shape pairing [13]. In the case of such pairings, the intraparietal sulcus and the parieto-occipital cortex are anatomical sites of convergence between the visual and auditory modality (see [2] for an overview).

The other audio-visual pairing which consists of emotional face-voice pairs has also been explored in behavioural as well as in neurophysiological research (see [16,17] for an overview). An fMRI study that directly addressed the neuro-anatomy of face-voice integration demonstrated that the amygdala and the fusiform gyrus were selectively activated in the case of fearful face-voice pairs [9]. When fearful faces were accompanied by fearful tone of voice an increase of the BOLD response was observed in these two brain regions and was not observed for happy pairings. These results suggest that the integration between a face and a voice is likely to be implemented in brain regions that do not overlap with areas (like the PPC) known to be involved in the integration of sound-shape pairs. By presenting the two pairs under similar testing conditions and keeping spatio-temporal constraints constant, interference effects of

TMS are related to the difference in semantic domain between the two pairs.

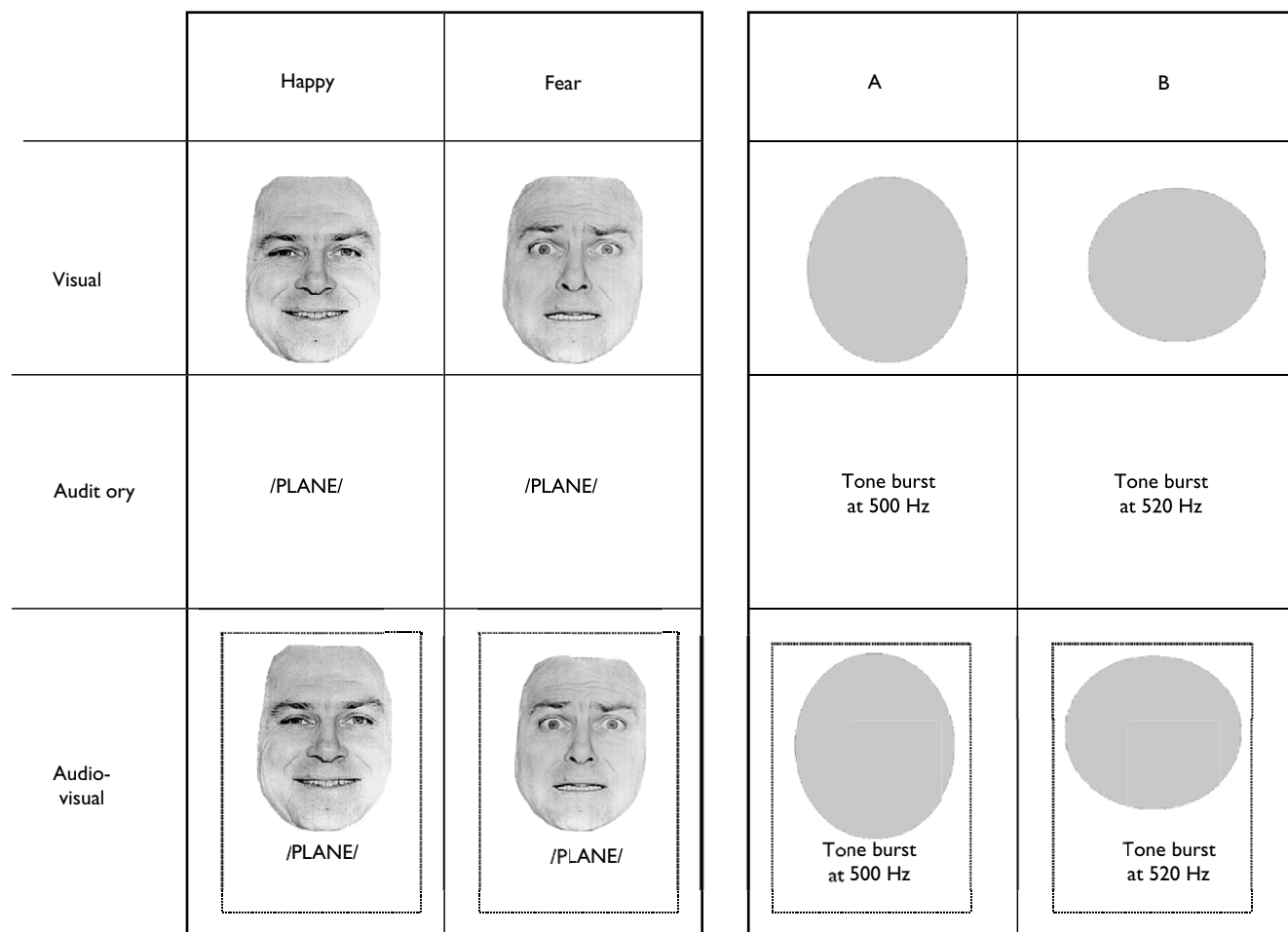
Our design used an object-discrimination task which allows to measure audio-visual interaction behaviourally. Evidence for audio-visual interaction is provided by a gain in accuracy and response latency for audio-visual trials compared to unimodal trials. With this task we can be confident that the effects observed are not simply due to post-perceptual factors as response competition (for further discussion on this issue, see [5,17]). Similar performance levels for the two types of pairs were obtained by introducing a training session for the arbitrary condition. After a brief training subjects treat sound-shape combinations as a single perceptual object and their performance characteristics indicate that there is perceptual integration indicated by faster and better responses for audio-visual trials than visual only or auditory only trials [18,19].

We tested the hypothesis that single-pulse TMS applied over right and left posterior parietal cortex (PPC) interferes with integration of sound-shape pairs but not of voice-face pairings. As a control condition, TMS was applied over the primary motor cortex (M1) in the right hemisphere. TMS induced interference of audio-visual integration was studied by triggering stimulation at two time intervals after stimulus presentation (100 or 200 ms). These latencies were selected based on behavioural [16] and electrophysiological results [15,20–22] previously obtained with similar stimulus pairs at these latencies.

## MATERIALS AND METHODS

**Participants:** Participants were nine right-handed adults (five males; mean age 25, range 22–27 years) who gave written consent after being informed about the TMS methods. The study was approved by the local ethical committee. All participants were screened for epilepsy and for the presence of metallic implants. All had normal or corrected to normal vision and no history of neurological problems.

**Apparatus, stimuli and procedure:** We used a magnetic stimulator (Magstim model 200) with a figure-of-eight coil with windings measuring 7 cm, producing a maximum output of 2 T. The centre of this coil produces the maximum electric field, and was therefore positioned perpendicularly to the cortical site to be stimulated. Participants wore an EEG cap and the PPC was located and marked on it on the left (P3 electrode position) and right (P4 electrode position) side of the head using the International 10–20 system [23]. Right M1 was detected for the scalp position where a visible twitch in the muscles of the contralateral left hand was elicited. TMS pulses were set at an intensity of 10% above the motor threshold defined as the TMS intensity that caused a visible twitch in the muscles of the left hand in 50% of the delivered pulses (three series of 10 pulses) over M1. In the voice-face condition stimuli consisted of facial expressions paired with voices (Fig. 1). The auditory stimulus was a neutral word (the word/plane/in French, *avion* /) spoken with either a happy or fearful tone of voice. The visual stimulus was a static picture of a face with either a happy or fearful expression [24]. In the arbitrary condition, the auditory stimulus was a tone burst produced either at



**Fig. 1.** Stimuli used for the voice-face and the sound-shape pairings.

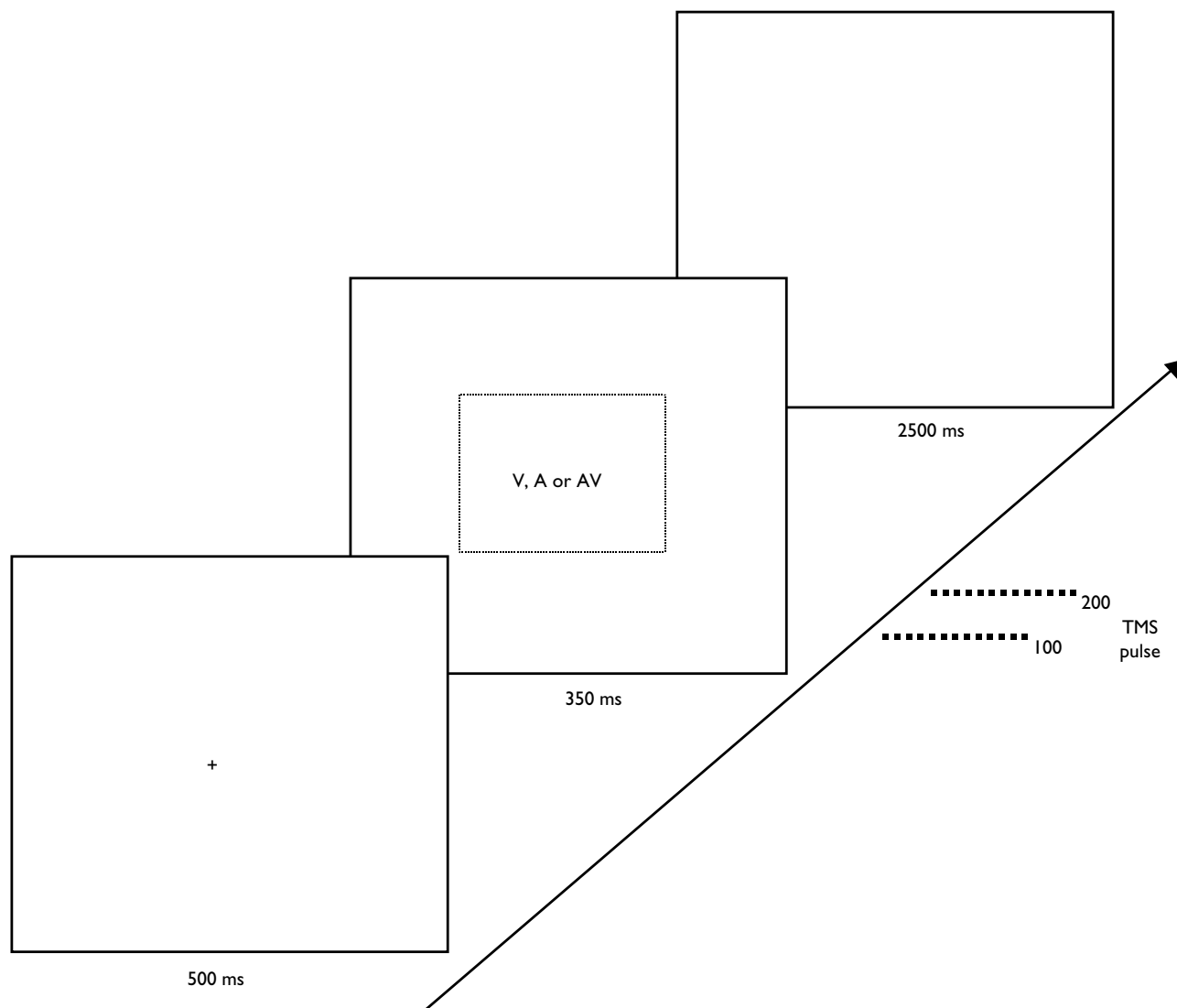
500 or 520 Hz. The visual stimulus was a geometrical shape either with a vertical or horizontal orientation (Fig. 1). The arbitrary audio-visual pairings were created by arbitrarily combining one shape with one tone (vertical ellipse with 500 Hz tone and horizontal ellipse with 520 Hz). The voice-face pairings consisted of a face expression and a spoken word with the same affective content. Physical stimulus properties, presentation modalities and task requirements of each condition were designed such as to be as similar as possible (luminance, mean size, duration and intensity). Mean size of visual stimuli was  $7 \times 9.5$  cm. Mean sound intensity was 73 dB. Each condition had three presentation modes (auditory only, visual only and audio-visual).

Onset and offset of visual and auditory stimuli of the audio-visual trials was synchronised. TMS-pulse was time-locked to the stimulus presentation with an asynchrony (SOA) of 100 or 200 ms (Fig. 2) using a CIO-DIO 24 card interface connecting the stimulator and the PC (Superlab software running on a PC Pentium 2). A trial started with a fixation cross (500 ms) followed by the stimulus presentation (350 ms). Mean duration of a trial was 3350 ms (Fig. 2). Inter-trial interval was 2500 ms. The time interval between two pulses was always  $> 3$  s, following the recommendations for the use of single pulse TMS [25]. The visual stimuli were displayed in the centre of a 17 inch screen

( $25 \times 32$  cm). The auditory stimuli were presented over two loudspeakers placed on each side of the computer screen.

Participants were instructed to make a two alternatives forced choice response (responding A *vs* B for the arbitrary condition or fear *vs* happy for the voice-face condition) by pressing the corresponding button on a response box with their dominant hand. For audio-visual trials, they were instructed to base their discrimination on the visual component of the pair. Accuracy as well as speed was stressed. Reaction times were recorded from stimulus onset. Participants were instructed to maintain fixation on the centre of the screen. An experimenter monitored eye movements. Participants were seated in a comfortable chair at a distance of 70 cm in front of the computer screen attending to the centre of the screen at eye level.

The experiment was preceded by a training phase. The goal of this training was to establish that performance specifically in the audio-visual trials was equally good for the two types of stimuli. Participants were first familiarised with the stimuli and procedure and subsequently received four training blocks. Errors were monitored and feedback was given. At the end of the training phase performance was  $> 80\%$  irrespective of type of pair, presentation modality and condition.



**Fig. 2.** Presentation conditions for the two different types of pairings.

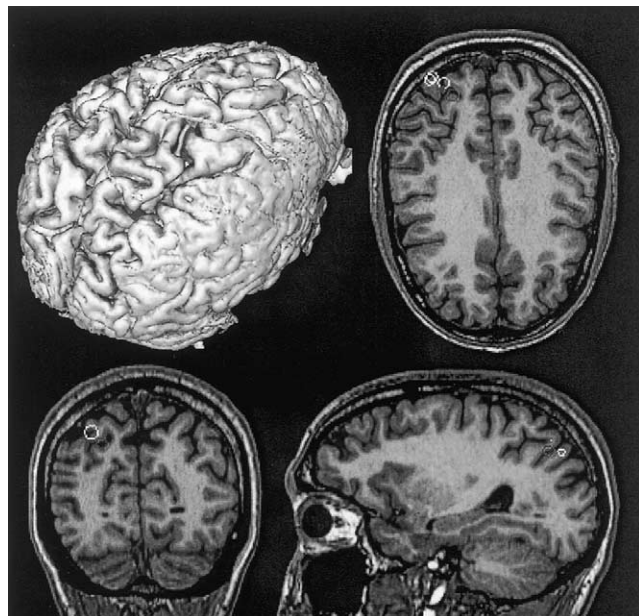
Following the training phase, participants were randomly presented with six different blocks (2 conditions  $\times$  3 sites), each of which was presented twice making a total of 12 blocks. In each block, 60 trials (3 modalities  $\times$  2 emotions/objects  $\times$  2 SOAs  $\times$  5 repetitions) were randomly presented.

The accurate localisation of TMS pulses was confirmed for two of nine subjects using a method that allows co-registration between TMS site and structural MRI (Fig. 3). The precise position of the coil was tracked with a 3D co-ordinates system (Polhemus Isotrak II system, Kaiser Aerospace Inc.). This system gives the x, y and z co-ordinates of each point relative to a fixed radio-frequency magnetic field transmitter. Stimulation sites were recorded with a digitizing receiver pen, relative to a second receiver fixed to the subject's forehead that allowed head movements. Then,  $\geq 60$  points were digitised over the scalp surface. This contour of the scalp was plotted in a 3D space and matched semi-automatically with the 3D reconstruction of the surface

of the head from MR images, using a software developed in the laboratory and based on the Visual Tool Kit (VTK) library. A transformation matrix was calculated, that computed any point of the 3D co-ordinate system into the MR system. Since position of the coil over P3, P4 and right M1 was digitised during the last trials, the transformation matrix allowed thus location of the coil relative to the head. A line was drawn from the centre of the coil through the scalp and skull until it crossed the brain surface. This cortical impact point was considered as the site where TMS was maximal. Depending on the cortical region of interest, co-registration accuracy of a few millimetres is attainable [26].

## RESULTS

**Accuracy:** Mean accuracy was  $> 85\%$  in all conditions independently of site of stimulation (right PPC, left PPC or right M1) or SOA between stimulus onset and pulse



**Fig. 3.** Co-registration between TMS and MR Images for one participant. Axial, sagittal, coronal sections and 3D reconstruction of brain surface showing the cortical sites (right parietal-P4) of magnetic stimulations. A beam perpendicular to the surface of the figure-of-8 coil was computed from the centre of the coil (beneath which the induced current is the strongest) and the impact point on the 3D-reconstructed cortical surface was considered the locus of stimulation. Each circle (sections) represents an impact point and the magenta cube (3D reconstruction) is the computed mean impact point.

triggering (100 or 200 ms; Table 1). In the arbitrary condition, a  $3$  (site)  $\times 2$  (stimulus A or B)  $\times 3$  (modalities)  $\times 2$  (SOA) ANOVA revealed a significant stimulus  $\times$  modality interaction ( $F(2,16) = 4.82$ ,  $p < 0.05$ ), indicating that participants made more errors with visual trials than audio-visual trials (and more errors with auditory trials than audio-visual trials only for stimulus A). In the voice-face condition, the ANOVA disclosed a significant effect of emotion ( $F(1,8) = 7.41$ ,  $p < 0.05$ ), indicating that participants made more errors with happy than fearful trials and a significant effect of SOA ( $F(1,8) = 6.82$ ,  $p = 0.05$ ), indicating that participants made more errors at 100 ms SOA than 200 ms SOA.

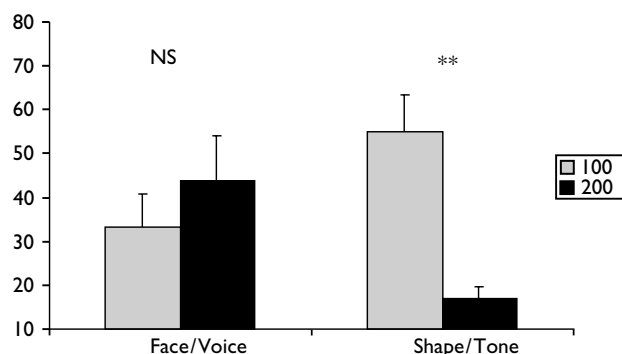
**Reaction times:** Reaction times for auditory trials were the slowest compared to visual or audio-visual trials (Table 2), independent of condition or SOA (100 or 200 ms). Statistical comparisons (repeated measures ANOVAs and Student paired  $t$ -tests) were made on the visual and audio-visual trials for each site of stimulation and each condition separately. As expected we found a significant interaction between modality (visual and audio-visual) and SOA (100 and 200 ms) only in the sound-shape condition and only for P3 scalp position ( $F(1,8) = 6.1$ ,  $p < 0.05$ ; Fig. 4). This effect was only observed when TMS was applied over the left PPC. It was not observed for stimulation over the right PPC ( $F(1,8) < 1$ ), nor when TMS was applied over right M1 ( $F(1,8) < 1$ ). Our results indicate that in the sound-shape condition when TMS was applied over the left PPC at 200 ms post-stimulus the latency advantage for audio-visual

**Table 1.** Mean ( $\pm$  s.e.) error rates (%) for the different conditions.

Condition	P3		P4		MI	
	100	200	100	200	100	200
Face-voice						
Auditory	10.0 $\pm$ 3.3	9.4 $\pm$ 3.8	12.8 $\pm$ 4.2	8.9 $\pm$ 3.5	13.3 $\pm$ 4.7	8.3 $\pm$ 3.9
Audio-visual	8.3 $\pm$ 2.4	6.7 $\pm$ 3.5	15.6 $\pm$ 4.5	10.6 $\pm$ 4.7	10.0 $\pm$ 3.8	8.9 $\pm$ 3.5
Visual	13.3 $\pm$ 3.4	8.9 $\pm$ 2.9	16.1 $\pm$ 4.8	12.2 $\pm$ 3.2	11.7 $\pm$ 4.5	11.1 $\pm$ 4.6
Shape-tone						
Auditory	6.1 $\pm$ 3.1	9.4 $\pm$ 4.0	12.2 $\pm$ 3.4	9.4 $\pm$ 3.7	11.7 $\pm$ 3.1	7.2 $\pm$ 2.8
Audio-visual	10.0 $\pm$ 3.3	6.1 $\pm$ 2.6	10.0 $\pm$ 4.9	5.6 $\pm$ 2.8	6.7 $\pm$ 4.1	7.2 $\pm$ 3.0
Visual	11.7 $\pm$ 2.9	16.1 $\pm$ 3.8	14.4 $\pm$ 4.5	9.4 $\pm$ 2.7	13.9 $\pm$ 3.6	8.9 $\pm$ 3.5

**Table 2.** Mean ( $\pm$  s.e.) reaction times (ms) for the different conditions.

Condition	P3		P4		MI	
	100	200	100	200	100	200
Face-voice						
Auditory	479.9 $\pm$ 13.2	498.9 $\pm$ 27.3	496.7 $\pm$ 27.9	500.1 $\pm$ 28.7	516.8 $\pm$ 32.2	506.8 $\pm$ 28.7
Audio-visual	420.9 $\pm$ 20.7	420.1 $\pm$ 19.0	426.1 $\pm$ 23.0	427.2 $\pm$ 17.5	436.8 $\pm$ 21.4	426.2 $\pm$ 20.1
Visual	454.2 $\pm$ 20.3	464 $\pm$ 22.9	472.7 $\pm$ 17.3	465 $\pm$ 20.8	458.3 $\pm$ 22.3	455.3 $\pm$ 22.7
Shape-tone						
Auditory	389.9 $\pm$ 31.7	410.6 $\pm$ 33.0	393.4 $\pm$ 35.9	430.2 $\pm$ 32.6	406.9 $\pm$ 38.0	414.7 $\pm$ 39.7
Audio-visual	314.6 $\pm$ 21.0	341.7 $\pm$ 15.6	332.4 $\pm$ 21.3	342.6 $\pm$ 18.8	321 $\pm$ 18.7	323.3 $\pm$ 13.6
Visual	369.5 $\pm$ 19.6	358.5 $\pm$ 16.3	379.2 $\pm$ 22.4	365.8 $\pm$ 19.3	358 $\pm$ 20.1	375.7 $\pm$ 18.4



**Fig. 4.** Reaction time difference (visual minus audio-visual trials) with standard error in ms in the face-voice and shape-tone conditions 100 and 200 ms post-stimulation onset when TMS was applied over the left PPC (P3 scalp position). \*\* $p < 0.05$  for interaction between SOA and modality.

trials compared to single modality trials was no longer significant ( $t(8) = 1.4$ ,  $p = 0.19$ ). The latency advantage for audio-visual *vs* visual only trials was highly significant at 100 ms SOA ( $t(8) = 4.9$ ,  $p < 0.005$ ), indicating faster reaction times in the audio-visual condition than in the single modality condition.

In the sound-shape condition, when TMS was applied over the left PPC, there was a linear loss of processing speed for audio-visual trials. This interaction was entirely due to a loss of processing speed in the audio-visual condition presumably occurring between 100 and 200 ms SOA ( $t(8) = 2.26$ ,  $p < 0.05$ ) and not to slower reaction times in the visual condition ( $t(8) = 1.1$ ,  $p = 0.29$ ).

In the voice-face condition no such interaction between modality and SOA was observed, whether TMS was applied over the same cortical region ( $F(1,8) < 1$ ), over the right M1 ( $F(1,8) = 1.65$ ,  $p = 0.24$ ) or over the right PPC ( $F(1,8) < 1$ ). In all three cases, the ANOVA revealed a significant effect of modality indicating faster reaction times for audio-visual trials than visual trials (for right M1,  $F(1,8) = 7.4$ ,  $p < 0.05$ ; for right PPC,  $F(1,8) = 25.14$ ,  $p < 0.001$ ; for left PPC,  $F(1,8) = 24.8$ ,  $p < 0.001$ ). When TMS was applied over the left PPC, at 200 ms post-stimulus, audio-visual trials were faster than single modality trials ( $t(8) = 3.41$ ,  $p < 0.01$ ).

## DISCUSSION

The goal of the present study was to illustrate the potential of TMS for understanding the role of semantic factors in multi-sensory perception thereby extending reports from brain-damaged patients. Our study is the first one to offer a comparative investigation of the impact on behavioural responses of single-pulse magnetic stimulation applied over frontal and parietal areas in an audio-visual task. Using two kinds of audio-visual pairings found in the literature, we tested the hypothesis that when TMS was applied over brain areas which were previously shown to be involved in inter-sensory integration, it would affect performance negatively. Our results indicate that when TMS is applied over the left PPC, the latency advantage for audio-visual trials over unimodal trials is significantly reduced specifically for sound-shape pairings. When TMS is applied over the left PPC, the modality (audio-visual or visual) interacts

with the moment in time the magnetic pulse is delivered (100 or 200 ms post-stimulus). As a consequence the relative speed advantage of audio-visual recognition over single modality trials is no longer significant at 200 ms. This significant interaction is entirely due to slower responses at 200 ms in the audio-visual condition.

The observation of an interference effect in the audio-visual condition at 200 ms post-stimulus onset is compatible with previous neurophysiological studies suggesting a role of the PPC in multimodal integration of sound-shape pairs at around that time window [13,15]. This interactive effect is not observed in the right hemisphere when TMS is applied over the homologue PPC or over the right primary motor cortex. Moreover, it is not observed in the voice-face condition whatever the scalp position (P3, P4 or right M1). The fact that the interference effect in the arbitrary condition is only observed for TMS applied over the left PPC is partly consistent with previous brain-imaging data, which have demonstrated bilateral activations in the parietal and temporal lobes but with larger and stronger effects in the left hemisphere than the right hemisphere during audio-visual integration [11,12]. It is plausible that TMS pulses delivered at a higher intensity over the right PPC (e.g. TMS pulses set at an intensity of 30% or 40% above the motor threshold) during audio-visual integration of arbitrary pairs would have created the same interference effect as observed for TMS applied over the left PPC. Further research focusing for example on task settings is needed to understand why this effect is lateralised to the left PPC.

Our results suggest that different neuro-anatomical pathways subserve the combined perception of voice-face *vs* sound-shape pairings that are presented under the same spatio-temporal constraints and with similar task requirements. Our data are consistent with recent results obtained with these two kinds of pairs previously studied using different techniques. A cortico-subcortical route for audio-visual integration of emotion was recently suggested in a study by Dolan and collaborators [9] using fMRI with normal participants. This pathway, including the amygdala and the fusiform gyrus may resist interference from TMS applied over posterior parietal heteromodal regions. Similarly, our data are consistent with involvement of the PPC for sound-shape pairs [12,13]. The TMS-MRI co-registration technique used here to visualise the putative location of the stimulation zone over the PPC indicated that the stimulation zone corresponded to the PPC (e.g. BA 7) near to the intraparietal sulcus (Fig. 3).

Finally, one might object that voice-face pairings may be more robust and better retained in memory and therefore better resist the kind of interference single-pulse TMS introduces. But if this would be the case, the effect of TMS will be the same at all stimulation sites.

## CONCLUSION

The contrast between voice-face and sound-shape pairings we explored here is a first step towards understanding how semantic factors like domain specificity contribute to audio-visual integration. Thus our data suggest that spatio-temporal contiguity of auditory and visual information is not the only determinant of cross-modal binding. Instead, our results raise the theoretical possibility that mechanisms

based on spatio-temporal contiguity and those based on content may interact. One interesting possibility is that pairings are based on spatio-temporal contiguity but that there is not a single neuronal site of audio-visual integration. Multiple neural sites of audio-visual integration may exist and bind appropriate audio-visual stimuli within spatio-temporal windows that are a function of the type of pairing. Single-pulse TMS appears a useful tool to unravel the complex phenomenon of multi-sensory integration by creating dissociations among different types of multi-sensory pairings that can only rarely be observed in patients with focal brain damage.

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